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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/416,920	04/21/1995	STEFAN MILTENYI	212302000320	1047

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EXAMINER
SCHWADRON, RONALD B

ART UNIT	PAPER NUMBER
1644	43

DATE MAILED: 10/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
08/416,920	Miltenyi et al.
Examiner	**Art Unit**
Ron Schwadron, Ph.D.	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL.** 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) ~~see office action~~ 71-74, 76-117, 119-244 is/are pending in the application.
99, 103, 108, 112, 113, 214, 218, 223, 233, 241

4a) Of the above, claim(s) ~~see office action~~ 145, 146, 155-159 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *see office action (too many to list here)* is/are rejected.

7)☒ Claim(s) *82-84, 88, 89, 125-127, 139, 140, 180-182, 198-200, 204, and 205* is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some* c)☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1. Since this application is eligible for the transitional procedure of 37 CFR 1.129(a), and the fee set forth in 37 CFR 1.17(r) has been timely paid, the finality of the previous Office action is hereby withdrawn pursuant to 37 CFR 1.129(a). Applicant's first submission after final filed on 10/30/2000 and subsequent amendments have been entered.

2. Newly submitted claims 112,113,145,146 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons.
The invention of claims 112,113,145,146 is drawn to genetically modified cells and methods of making said cells classified in Class 435, subclass 362. The previously examined invention is drawn to cells and methods classified in Class 435, subclass 326. These cells are structurally and functionally different wherein one cell population contains recombinant nucleic acids and the other does not.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 112,113,145,146 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

3. Applicant's election of the species elected in in Paper no. 39 and 37 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse. See MPEP section § 818.03(a)).

4. Claims 99,103,108,112,113,145,146,155-159,214,218,223,233,241 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species. Election was made without traverse in Paper No. 39 and 37.

The nonelected species related to the method claims have been rejoined because the method claims are free of prior art.

5. Claims 71-74,76-98,100-102,104-107,109-111,114-117,119-144,147-154,160-213,215-217,219-222,224-232,234-240,242-244 are under consideration.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 151,166,168-171,231,239 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support in the specification as originally filed for the kit of claim 151 which recites "medium for cell incubation". Regarding applicants comments about the specification, page 18, lines 9-33, said passage discloses use of viscous or gelatinous media or use of latex beads conjugated to an antibody. It does not disclose use of "medium for cell incubation" per se because said term would encompass media other than viscous or gelatinous media and the use of such media in the claimed kit is not disclosed in the specification as originally filed.

There is no support in the specification as originally filed for the kit of claim 166/231/239 which recites use of biotin/avidin. Regarding applicants comments about the specification, page 15, lines 11-14, said passage discloses use of avidin attached to a hydrophobic anchor moiety with biotin labeled antibody. It does not disclose use of the avidin biotin system per se because it only discloses use of avidin biotin attached to the aforementioned specific molecules.

There is no support in the specification as originally filed for the method of claims 168. Regarding applicants comments, the only method disclosed in the specification for determining the amount of cells labeled in a population is the method of original claim 31 which includes additional steps not recited in claim 168.

There is no support in the specification as originally filed for the scope of the claimed inventions (eg. the claimed inventions constitute new matter).

8. Claims 71-74,76-81,85-87,90-98,101,102,104-107,114-117,119-124,128-138,141-144,147-154,160-179,183-197,201-203,206-213,216,217,219-222,227-232,234-240,242,243,244 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of the claimed inventions.

The instant claims encompass products, kits or methods wherein the capture moiety is "coupled" to cells or attached via a "anchor moiety". The only procedures disclosed in the specification for coupling a capture moiety to a cell/anchoring moieties for attaching a capture moiety to a cell are direct chemical coupling via traditional organic chemistry methods, or use of fatty acids or antibodies or lectins. The terms "coupled" to cells or attached via a "anchor moiety" would encompass a potentially large genus of undisclosed reagents for coupling/anchor moieties to attach the capture reagent to the cell surface. For example, use of a vast array of ligand/receptor systems other than antibody (eg. MHC binding agents, TCR binding agents) which are not disclosed in the specification. It would encompass use of nonprotein binding agents not disclosed in the specification (eg. carbohydrates that bind cell surface receptors). With the exception of the aforementioned disclosed coupling/anchoring moieties, the skilled artisan cannot envision the detailed structure of the encompassed reagents and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. In the instant application, the amino acid itself or isolated protein is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

In view of the aforementioned problems regarding description of the claimed invention, the specification does not provide an adequate written description of the invention claimed herein. See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1404-7 (Fed. Cir. 1997). In University of California v. Eli Lilly and Co., 39 U.S.P.Q.2d 1225 (Fed. Cir. 1995) the inventors claimed a genus of DNA species encoding insulin in different vertebrates or mammals, but had only described a single species of cDNA which encoded rat insulin. The court held that only the nucleic acids species described in the specification (i.e. nucleic acids encoding rat insulin) met the description requirement and that the inventors were not

entitled to a claim encompassing a genus of nucleic acids encoding insulin from other vertebrates, mammals or humans, id. at 1240. In the instant case, the specification has only disclosed procedures for coupling a capture moiety to a cell/anchoring moieties for attaching a capture moiety to a cell are direct chemical coupling via traditional organic chemistry methods, or use of fatty acids or antibodies or lectins. The terms "coupled" to cells or attached via a "anchor moiety" would encompass a potentially large genus of undisclosed reagents for coupling/anchor moieties to attach the capture reagent to the cell surface. The Federal Circuit has held that if an inventor is "unable to envision the detailed constitution of a gene so as to distinguish it from other materials. . .conception has not been achieved until reduction to practice has occurred", Amgen, Inc. v. Chugai Pharmaceutical Co, Ltd., 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991). Attention is also directed to the decision of The Regents of the University of California v. Eli Lilly and Company (CAFC, July 1997) wherein is stated:
"The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, as we have previously held, a cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA." See Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 93-95,101,104,106,107,109,147-149,209,210,216,219,221,222,224 are rejected

under 35 U.S.C. § 102(b) as being clearly anticipated by Kohler et al.

Kohler et al. teach direct coupling of TNP to hybridomas which secrete IgM specific for TNP (see section 2.8, page 469). Said cells express cell surface markers recited in the claims such as CD45 and MHC class I because the art recognizes that said markers are found on B cells. Kohler et al. teach that said clones are subsequently incubated with specific anti-mouse-υ serum (see page 471, second column, section 3.3). Said serum would bind the captured IgM because IgM contains υ chain. The recitation of a method wherein the instant product is made carries no patentable weight in this product claim because the claimed product is the same as the product of the prior art.

Applicants comments are addressed in this new art rejection.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 93-98,100-102,104-107,109-111,147-149,209-213,215-217,219-222,224-226 are rejected under 35 U.S.C. § 103 as being unpatentable over Kohler et al in view of Segal (US Patent 4,676,980) and Brennan et al.

Kohler et al. teach direct coupling of TNP to hybridomas which secrete IGM specific for TNP (see section 2.8, page 469). Said cells express cell surface markers recited in the claims such as CD45 and MHC class I because the art recognizes that said markers are found on B cells. Kohler et al. teach that said clones are subsequently incubated with specific anti-mouse-υ serum. Said serum would bind the captured IgM because IgM contains υ chain. The recitation of a method wherein the instant product is made carries no patentable weight in this product claim because the claimed product is the same as the product of the prior art. Kohler et al. do not teach the compositions of claims 96/211, 97/212,98/213,100/215,102/217,105/220, 110/225 or 111/226. Segal teaches bispecific antibodies (see Abstract). Segal teaches that bispecific antibodies can bind a cell surface antigen on the surface of a target cell and also bind another desired antigen, thus bringing the antigen to the cell surface (see columns 1 and 2). A routineer would used bispecific antibodies which bind any art known molecule that exists on the surface of a desired target cell.

A routineer would have used any desired capturing probe instead of TNP, including an antibody and would have attached the antibody to the cell surface using any art known procedure including those utilizing linking agents. Use of fluorescinated antibodies in immunoassays is well known in the art. Brennan et al. teach the use of bispecific antibodies in immunoassays (see page 81, column 2). Brennan et al. teach that bispecific antibodies can be used to link two different molecules (see page 83, last paragraph, first column, continued on next column). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Kohler et al. teach the claimed invention except for use of a bispecific antibody, while Segal teaches that bispecific antibodies can bind a cell surface antigen on the surface of a target cell and also bind another desired antigen, and Brennan et al. teach that bispecific antibodies can be used to link two different molecules. A routineer would have created cells which bound any particular secreted molecule (such as IFN-γ) for use in the selection of functional mutants which produce said molecule as per Kohler et al. Segal et al. teach that the bispecific antibody (eg. capture moiety/anchor moiety) can be formed by joining an avidin labeled antibody of one specificity to a second antibody having a different specificity (see column 5). The use of dextran as a linking agent is well known in the art.

13. Claims 150-154,160-166,227-232,234-240,242,243 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kohler et al in view of Segal (US Patent 4,676,980) and Brennan et al. as applied to claims 93-98,100-102,104-107,109-111,147-149,209-213,215-217,219-222,224-226 above, and further in view of Zuk et al (U.S. Patent No. 4,281,061).

The previous rejection renders obvious the claimed invention except for a kit containing the aforementioned reagents. Zuk et al. teach that reagents for an immunoassay can be provided as kits as a matter of convenience and to optimize the sensitivity of the assay in the range of interest (col 22, line 62 - col 23, line 4).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to include the necessary reagents to perform the immunoassay in a kit format for the convenience and economy of the user.

14. Claims 82-84,88,89,125-127,139,140,180-182.198-200,204,205 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 1600 at (703) 308-4242

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Monday through Thursday from 7:30 to 6:00. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP 1800

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644